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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|-----------------------|---------------------|------------------|
| 10/743,391 | 12/22/2003 | Timothy Raymond Hirst | 00833-P0043A | 7178 |
| 24126 7590 03/20/2008 ST. ONGE STEWARD JOHNSTON & REENS, LLC 986 BEDFORD STREET STAMFORD, CT 06905-5619 | | | | |
| EXAMINER MONTANARI, DAVID A | | | | |
| ART UNIT | | PAPER NUMBER | | |
| 1632 | | | | |
| MAIL DATE | | DELIVERY MODE | | |
| 03/20/2008 | | PAPER | | |

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

**Advisory Action
Before the Filing of an Appeal Brief**

| | |
|--------------------------------------|---|
| Application No. 10/743,391 | Applicant(s) HIRST, TIMOTHY RAYMOND |
| Examiner DAVID MONTANARI | Art Unit 1632 |

--The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

THE REPLY FILED 08 February 2008 FAILS TO PLACE THIS APPLICATION IN CONDITION FOR ALLOWANCE.

1. ☒ The reply was filed after a final rejection, but prior to or on the same day as filing a Notice of Appeal. To avoid abandonment of this application, applicant must timely file one of the following replies: (1) an amendment, affidavit, or other evidence, which places the application in condition for allowance; (2) a Notice of Appeal (with appeal fee) in compliance with 37 CFR 41.31; or (3) a Request for Continued Examination (RCE) in compliance with 37 CFR 1.114. The reply must be filed within one of the following time periods:

- a) ☐ The period for reply expires _____ months from the mailing date of the final rejection.
b) ☒ The period for reply expires on: (1) the mailing date of this Advisory Action, or (2) the date set forth in the final rejection, whichever is later. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of the final rejection.
Examiner Note: If box 1 is checked, check either box (a) or (b). ONLY CHECK BOX (b) WHEN THE FIRST REPLY WAS FILED WITHIN TWO MONTHS OF THE FINAL REJECTION. See MPEP 706.07(f).

Extensions of time may be obtained under 37 CFR 1.136(a). The date on which the petition under 37 CFR 1.136(a) and the appropriate extension fee have been filed is the date for purposes of determining the period of extension and the corresponding amount of the fee. The appropriate extension fee under 37 CFR 1.17(a) is calculated from: (1) the expiration date of the shortened statutory period for reply originally set in the final Office action; or (2) as set forth in (b) above, if checked. Any reply received by the Office later than three months after the mailing date of the final rejection, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

NOTICE OF APPEAL

2. ☐ The Notice of Appeal was filed on _____. A brief in compliance with 37 CFR 41.37 must be filed within two months of the date of filing the Notice of Appeal (37 CFR 41.37(a)), or any extension thereof (37 CFR 41.37(e)), to avoid dismissal of the appeal. Since a Notice of Appeal has been filed, any reply must be filed within the time period set forth in 37 CFR 41.37(a).

AMENDMENTS

3. ☐ The proposed amendment(s) filed after a final rejection, but prior to the date of filing a brief, will not be entered because
(a) ☐ They raise new issues that would require further consideration and/or search (see NOTE below);
(b) ☐ They raise the issue of new matter (see NOTE below);
(c) ☐ They are not deemed to place the application in better form for appeal by materially reducing or simplifying the issues for appeal; and/or
(d) ☐ They present additional claims without canceling a corresponding number of finally rejected claims.
NOTE: _____. (See 37 CFR 1.116 and 41.33(a)).

4. ☐ The amendments are not in compliance with 37 CFR 1.121. See attached Notice of Non-Compliant Amendment (PTOL-324).
5. ☒ Applicant's reply has overcome the following rejection(s): 35 USC 112, first paragraph, scope of enablement.
6. ☐ Newly proposed or amended claim(s) _____ would be allowable if submitted in a separate, timely filed amendment canceling the non-allowable claim(s).
7. ☒ For purposes of appeal, the proposed amendment(s): a) ☐ will not be entered, or b) ☒ will be entered and an explanation of how the new or amended claims would be rejected is provided below or appended.
The status of the claim(s) is (or will be) as follows:
Claim(s) allowed: NONE.
Claim(s) objected to: NONE.
Claim(s) rejected: 1-3, 10, 11, 17, 18, 21, 26 and 27.
Claim(s) withdrawn from consideration: NONE.

AFFIDAVIT OR OTHER EVIDENCE

8. ☐ The affidavit or other evidence filed after a final action, but before or on the date of filing a Notice of Appeal will not be entered because applicant failed to provide a showing of good and sufficient reasons why the affidavit or other evidence is necessary and was not earlier presented. See 37 CFR 1.116(e).
9. ☐ The affidavit or other evidence filed after the date of filing a Notice of Appeal, but prior to the date of filing a brief, will not be entered because the affidavit or other evidence failed to overcome all rejections under appeal and/or appellant fails to provide a showing a good and sufficient reasons why it is necessary and was not earlier presented. See 37 CFR 41.33(d)(1).
10. ☐ The affidavit or other evidence is entered. An explanation of the status of the claims after entry is below or attached.

REQUEST FOR RECONSIDERATION/OTHER

11. ☒ The request for reconsideration has been considered but does NOT place the application in condition for allowance because:
See Continuation Sheet.
12. ☐ Note the attached Information Disclosure Statement(s). (PTO/SB/08) Paper No(s). _____
13. ☐ Other: _____.

/Peter Paras, Jr./
Supervisory Patent Examiner, Art Unit 1632

Continuation of 11, does NOT place the application in condition for allowance because: while Applicant has amended the claims to a method carried out in vitro, thus overcoming the 35 USC, 112 first paragraph rejection, an issue remains about the proper sequence identifiers for the sequences present in the instant claims.

Applicants filed on 9/4/2007 a new Sequence Listing, however it is unclear as the claims are presently written that SEQ ID NO: 13 includes the E51A and Q56A mutations in CtxB. It is clear from the sequence listing that they are contained within SEQ ID NO: 13 however this is not clear in the claims. Currently SEQ ID NO: 13 follows only H57A in line 8 of claim 1 (also line 5 of claim 12, line 9 of claim 17 and line 6 of claim 21) and would imply that SEQ ID NO: 13 only applies to H57A. Applicant is invited to amend the instant claims to clarify that the 3 single point mutations in CtxB are all contained within SEQ ID NO: 13.

There exists a separate issue with EtxB (H57S) and its proper sequence identifier. See pages 4 of the amendment filed on 9/4/2007. The entry at SEQ ID NO: 16 says it is "Mutant EtxB (H57A)" however it is not apparent if this is a typographical error and should be H57S, since it is noted that EtxB H57A is not recited in the claims. Further a sequence identifier for EtxB (H57S) must be present in the claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to DAVID MONTANARI whose telephone number is (571)272-3108. The examiner can normally be reached on M-Tr 8-6.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 1-571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

David A. Montanari, Ph.D.
AU1632